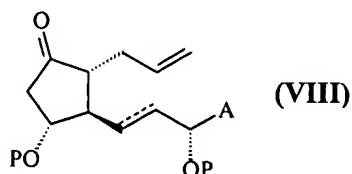
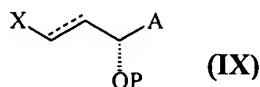


Claims

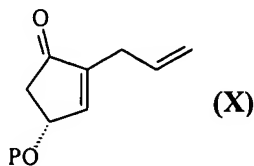
1. A process for the preparation of a compound of formula (VIII):



- 5 wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group
- 10 consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group; and ----- represents a double bond or a single bond; comprising converting a compound of formula (IX):



- wherein A, P and ----- are as defined above and X is a leaving group, to a cuprate
- 15 reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (X):

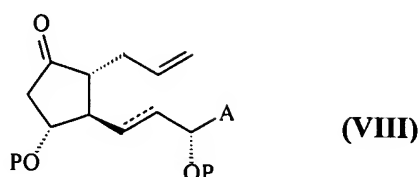


wherein P is as defined above.

- 20 2. The process according to claim 1, wherein P is a tetrahydropyranyl (THP) protecting group.
3. The process according to claim 1 or claim 2, wherein X is iodine.

4. The process according to claim 1, wherein A is $(\text{CH}_2)_2\text{Ph}$, ----- represents a double bond, P is THP and X is I.

5. A compound of formula (VIII):



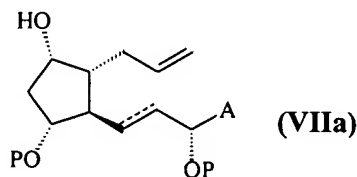
5

wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and $(\text{CH}_2)_n\text{OR}'$ wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group; and ----- represents a double bond or a single bond.

6. The compound according to claim 5, wherein A is $(\text{CH}_2)_2\text{Ph}$, ----- represents a double bond and P is THP.

15

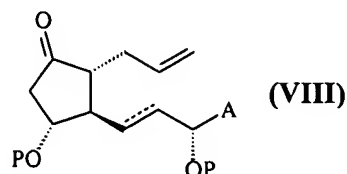
7. A process for the preparation of a compound of formula (VIIa):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and $(\text{CH}_2)_n\text{OR}'$ wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group and ----- represents a double bond or a single bond;

25

comprising selectively reducing a compound of formula (VIII):



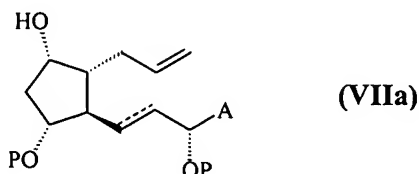
wherein A, P and ----- are as defined above.

8. The process according to claim 7, wherein P is a tetrahydropyranyl (THP) protecting group.

9. The process according to claim 7, wherein A is $(\text{CH}_2)_2\text{Ph}$, ----- represents a double bond and P is THP.

10

10. A compound of formula (VIIa):



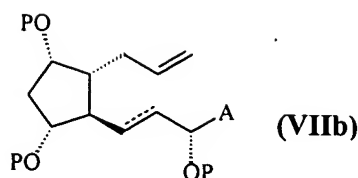
;

wherein A is selected from the group consisting of $\text{C}_1\text{-C}_6$ alkyl groups; $\text{C}_7\text{-C}_{16}$ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of $\text{C}_1\text{-C}_6$ alkyl groups, halo and CF_3 ; and $(\text{CH}_2)_n\text{OR}'$ wherein n is an integer from 1 to 3 and R' represents a $\text{C}_6\text{-C}_{10}$ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of $\text{C}_1\text{-C}_6$ alkyl groups, halo and CF_3 ; P is a hydroxyl protecting group; and ----- represents a double bond or a single bond.

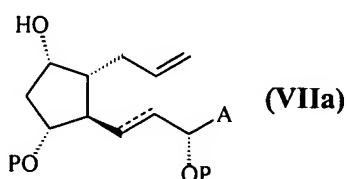
20

11. The compound according to claim 10, wherein A is $(\text{CH}_2)_2\text{Ph}$, ----- represents a double bond and P is THP.

12. A process for the preparation of a compound of formula (VIIb):



- wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group and ----- represents a double bond or a single bond; comprising protecting a compound of formula (VIIa):

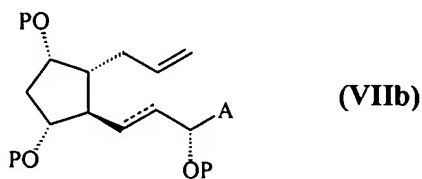


wherein A, P and ----- are as defined above, with a hydroxyl protecting group.

13. The process according to claim 12, wherein P is a tetrahydropyranyl (THP) protecting group.

14. The process according to claim 12, wherein A is (CH₂)₂Ph, ----- represents a double bond and P is THP.

15. A compound of formula (VIIb):

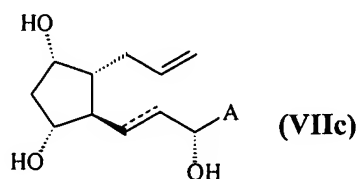


wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three

substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group;
 5 and ----- represents a double bond or a single bond.

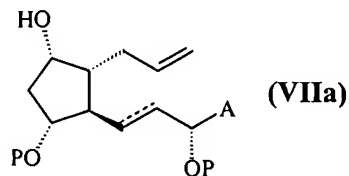
16. The compound according to claim 15, wherein A is (CH₂)₂Ph, ----- represents a double bond and P is THP.

10 17. A process for the preparation of a compound of formula (VIIc):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and
 15 (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃ and ----- represents a double bond or a single bond;

comprising deprotecting a compound of formula (VIIa):



20

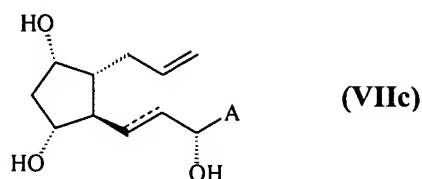
wherein A and ----- are as defined above and P is a protecting group.

18. The process according to claim 17, wherein P is a tetrahydropyranyl (THP) protecting group.

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19. The process according to claim 17 or claim 18, wherein A is $(\text{CH}_2)_2\text{Ph}$ and ===== represents a double bond.

20. A compound of formula (VIIc):



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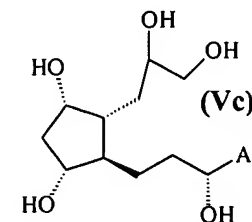
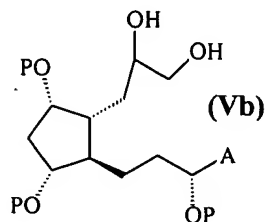
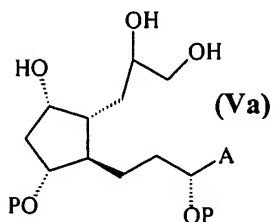
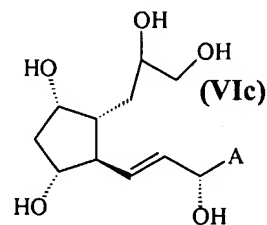
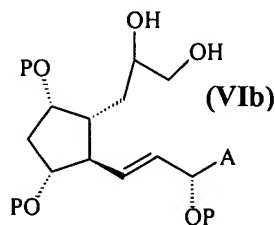
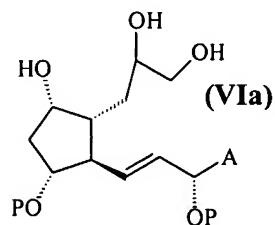
wherein A is selected from the group consisting of $\text{C}_1\text{-C}_6$ alkyl groups; $\text{C}_7\text{-C}_{16}$ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of $\text{C}_1\text{-C}_6$ alkyl groups, halo and CF_3 ; and $(\text{CH}_2)_n\text{OR}'$ wherein n is an integer from 1 to 3 and R' represents a $\text{C}_6\text{-C}_{10}$ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of $\text{C}_1\text{-C}_6$ alkyl groups, halo and CF_3 ; P is a hydroxyl protecting group; and ===== represents a double bond or a single bond.

10

21. The compound according to claim 20, wherein A is $(\text{CH}_2)_2\text{Ph}$ and ===== represents a double bond.

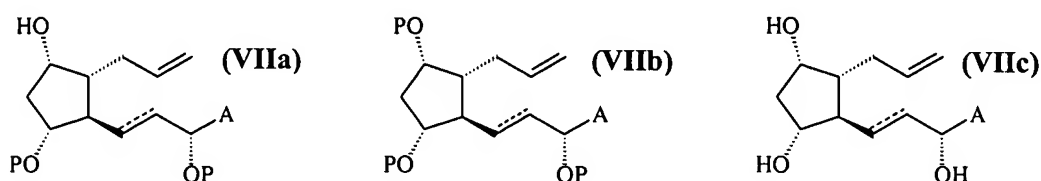
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22. A process for the preparation of a compound of formula (VIa), (VIb), (VIc), (Va), (Vb) or (Vc):



20

wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and P is a hydroxyl protecting group; comprising dihydroxylating a compound of formula (VIIa), a compound of formula (VIIb) or a compound of formula (VIIc):



wherein A and P are as defined above and ----- is a double or single bond.

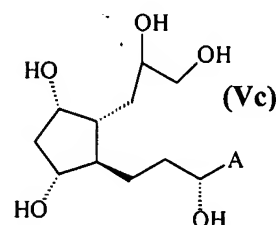
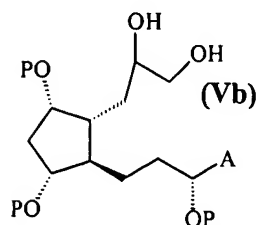
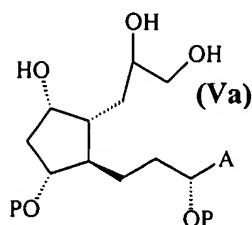
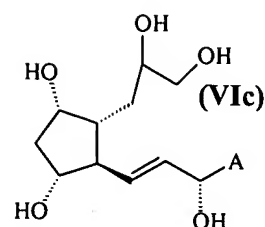
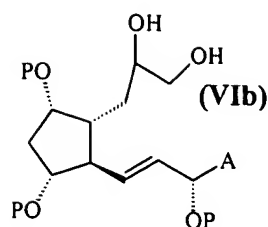
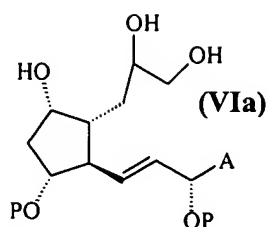
23. The process according to claim 22, wherein P is a tetrahydropyranyl (THP) protecting group.


24. The process according to claim 22, wherein A is (CH₂)₂Ph, P is THP, ----- represents a double bond, and compound (VIIa) reacts to give compound (VIa).

25. The process according to claim 22, wherein A is (CH₂)₂Ph, P is THP, ----- represents a double bond, and compound (VIIb) reacts to give compound (VIb).

26. The process according to claim 22, wherein A is (CH₂)₂Ph, ----- represents a double bond, and compound (VIIc) reacts to give compound (VIc).

27. A compound of formula (VIa), (VIb) (VIc), (Va), (Vb) or (Vc):

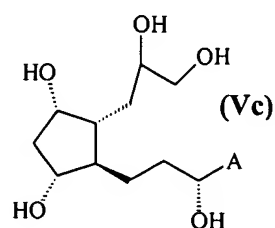
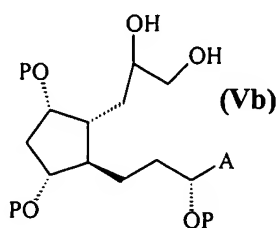
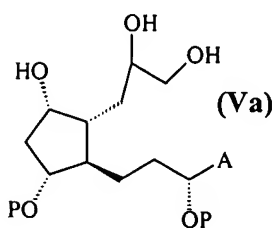


wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group; and  represents a double bond or a single bond.

10

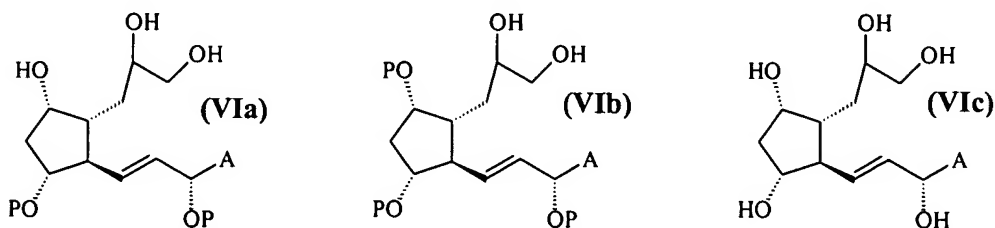
28. The compound according to claim 27, wherein A is (CH₂)₂Ph and P is THP.

29. A process for the preparation of a compound of formula (Va), (Vb) or (Vc):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which

is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and P is a hydroxyl protecting group; comprising reducing a double bond of a compound of formula (VIa), a compound of formula (VIb) or a compound of formula (VIc):



wherein A and P are as defined above.

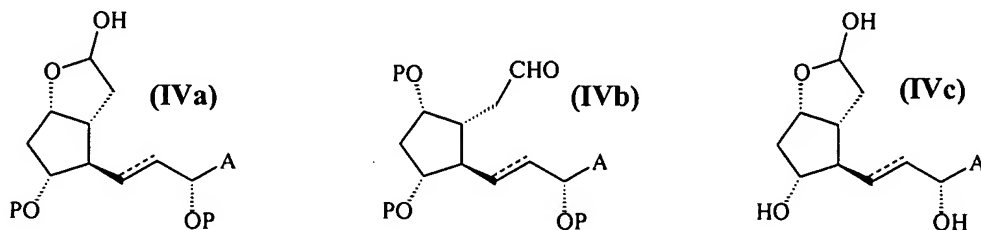
30. The process according to claim 29, wherein P is a tetrahydropyranyl (THP) protecting group.

31. The process according to claim 29, wherein A is (CH₂)₂Ph, P is THP and compound (VIa) reacts to give compound (Va).

32. The process according to claim 29, wherein A is (CH₂)₂Ph, P is THP and compound (VIb) reacts to give compound (Vb).

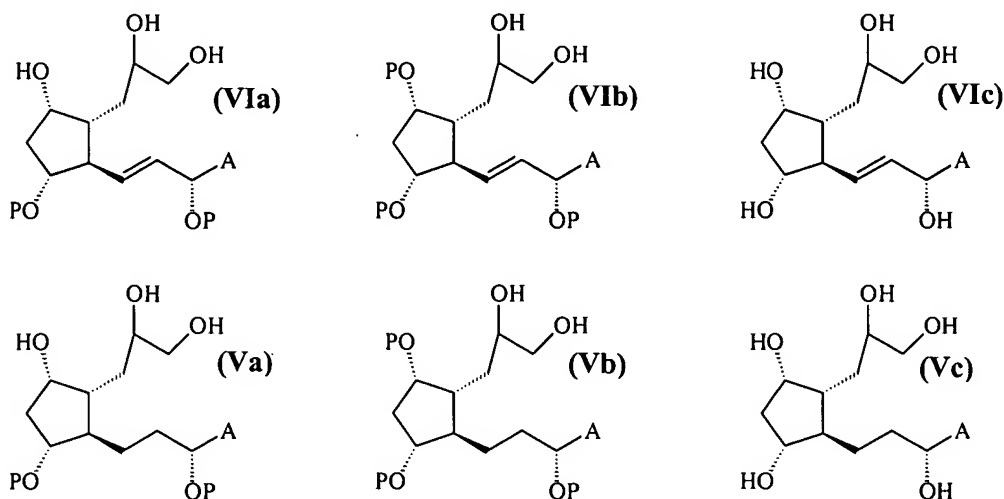
33. The process according to claim 29, wherein A is (CH₂)₂Ph and compound (VIc) reacts to give compound (Vc).

34. A process for the preparation of a compound of formula (IVa), (IVb) or (IVc):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three

substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group and ----- represents a double bond or a single bond; comprising performing a diol cleavage reaction on a compound of formula (VIa), (Va), (VIb), (Vb), (VIc) or (Vc):



wherein A and P are as defined above.

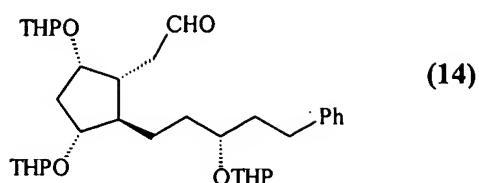
35. The process according to claim 34, wherein P is a tetrahydropyranyl (THP) protecting group.

36. The process according to claim 34, wherein A is (CH₂)₂Ph, P is THP, ----- represents a single bond, and compound (Va) reacts to give compound (IVa).

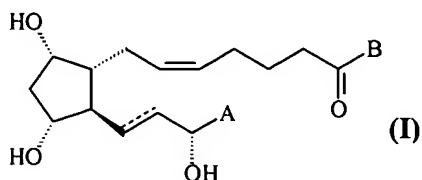
37. The process according to claim 34, wherein A is (CH₂)₂Ph, P is THP, ----- represents a single bond, and compound (Vb) reacts to give compound (IVb).

38. The process according to claim 34, wherein A is (CH₂)₂Ph, ----- represents a single bond, and compound (Vc) reacts to give compound (IVc).

39. A compound having the formula (14):



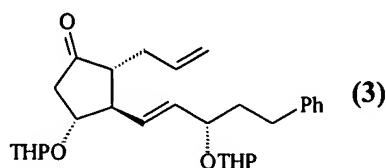
40. A process for the preparation of a prostaglandin compound having the formula (I):



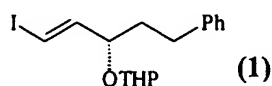
5 wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group
10 consisting of C₁-C₆ alkyl groups, halo and CF₃; B is selected from OR" and NHR" wherein R" is C₁-C₆ alkyl groups; and ----- represents a double bond or a single bond; comprising a process according to any one of claims 1, 2, 4, 7-9, 12-14, 17, 18, 22-26 and 29-38.

15 41. A process for synthesising Latanoprost comprising the steps of:

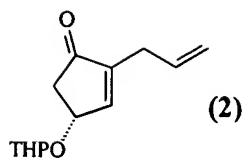
a) preparing a compound of formula (3):



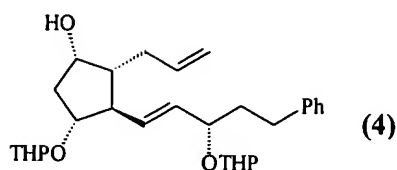
said preparing comprising converting a compound of formula (1):



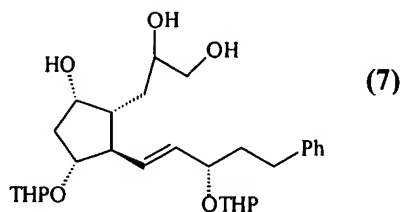
20 to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent
and a compound of formula (2):



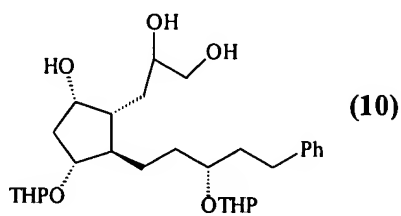
b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



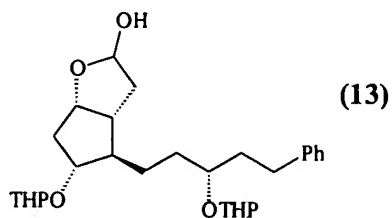
5 c) dihydroxylating the compound of formula (4) to provide a compound of formula (7):



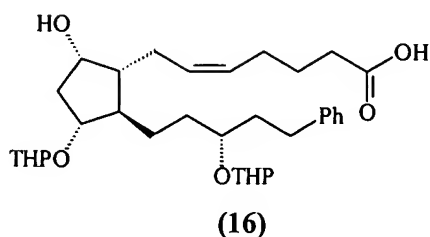
d) reducing the compound of formula (7) to provide a compound of formula (10):



10 e) performing a diol cleavage reaction on the compound of formula (10) to provide a compound formula (13):

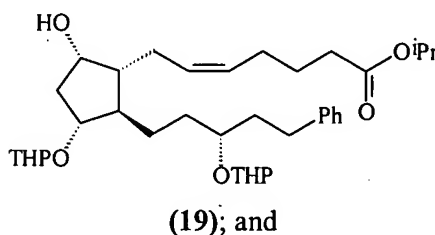


f) performing a Wittig reaction on the compound of formula (13) to provide a compound of formula (16):



5

g) esterifying the compound of formula (16) to provide a compound of formula (19):

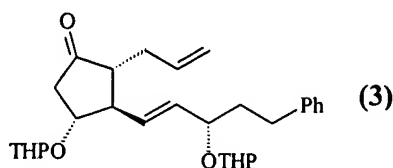


10

h) deprotecting the compound of formula (19) to provide Latanoprost.

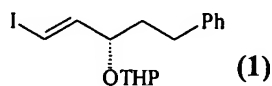
42. A process for synthesising Latanoprost comprising the steps of:

a) preparing a compound of formula (3):

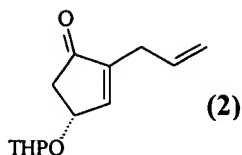


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said preparing comprising converting a compound of formula (1):

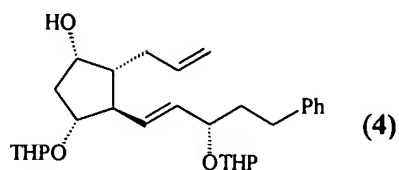


to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



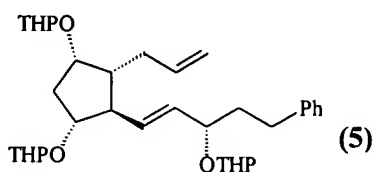
;

b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



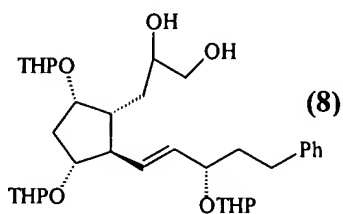
;

5 c) protecting the compound of formula (4) to provide a compound of formula (5):



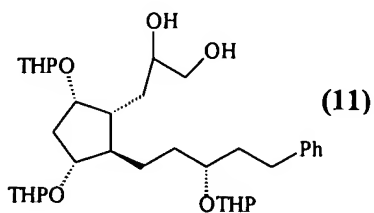
;

d) dihydroxylating the compound of formula (5) to provide a compound of formula (8):



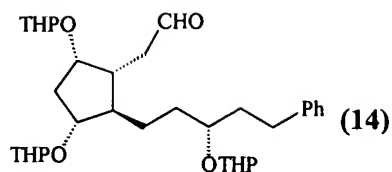
;

10 e) reducing the compound of formula (8) to provide a compound of formula (11):



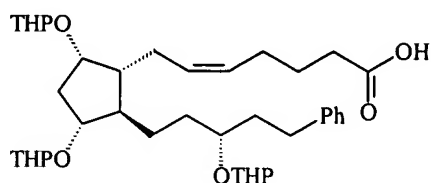
;

f) performing a diol cleavage reaction on the compound of formula (11) to provide a compound of formula (14):

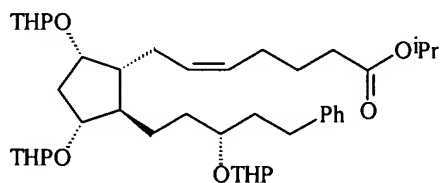


;

g) performing a Wittig reaction on the compound of formula (14) to provide a compound of formula (17):



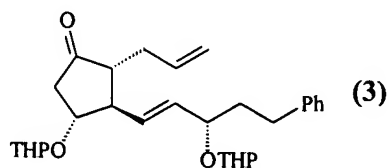
h) esterifying the compound of formula (17) to provide a compound of formula (20):



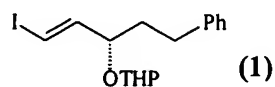
i) deprotecting the compound of formula (20) to provide Latanoprost.

43. A process for synthesising Latanoprost comprising the steps of:

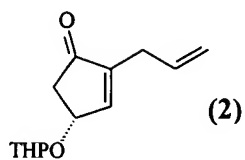
a) preparing a compound of formula (3):



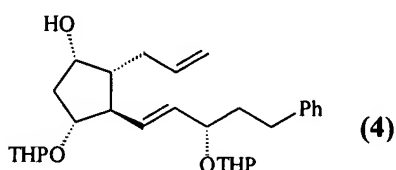
said preparing comprising converting a compound of formula (1):



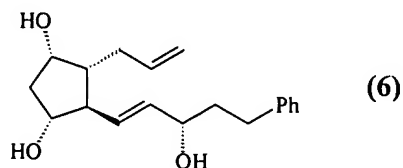
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



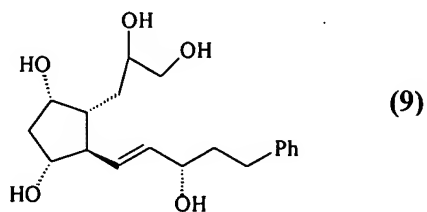
- b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



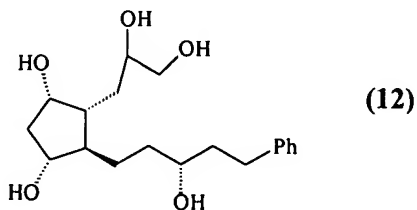
- c) deprotecting the compound of formula (4) to provide a compound of formula (6):



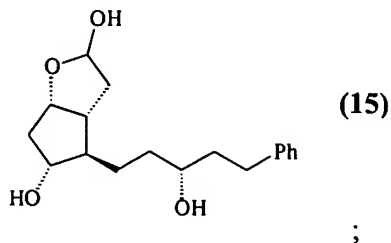
- d) dihydroxylating the compound of formula (6) to provide a compound of formula (9):



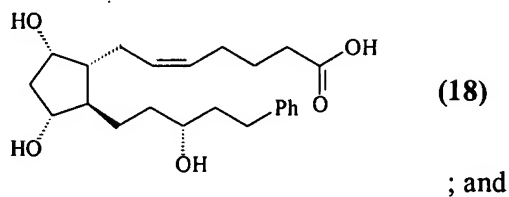
- e) reducing the compound of formula (9) to provide a compound of formula (12):



f) performing a diol cleavage reaction on the compound of formula (12) to provide a compound of formula (15):



5 g) performing a Wittig reaction on the compound of formula (15) to provide a compound of formula (18):

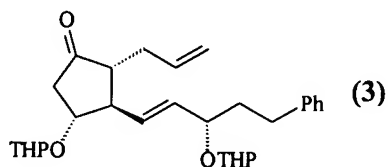


h) esterifying the compound of formula (18) to provide Latanoprost.

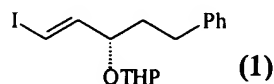
10

44. A process for synthesising Bimatoprost comprising the steps of:

a) preparing a compound of formula (3):

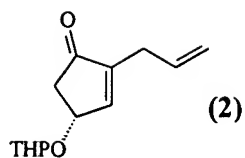


said preparing comprising converting a compound of formula (1):



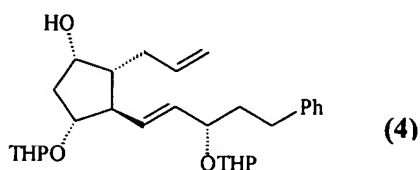
15

to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



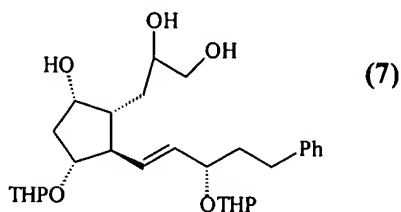
;

b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



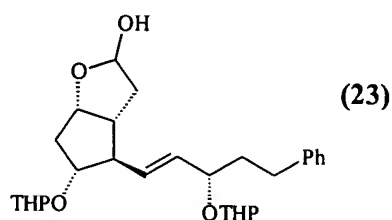
;

5 c) dihydroxylating the compound of formula (4) to provide a compound of formula (7):



;

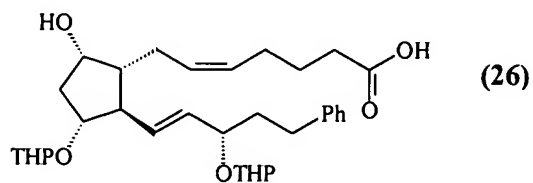
d) performing a diol cleavage reaction on the compound of formula (7) to provide a compound of formula (23):



;

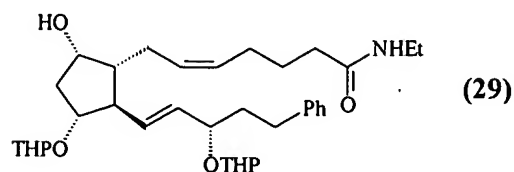
10

e) performing a Wittig reaction on the compound of formula (23) to provide a compound of formula (26):



;

- f) amidating the compound of formula (26) to provide a compound of formula (29):

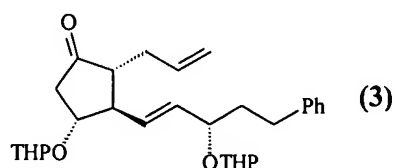


; and

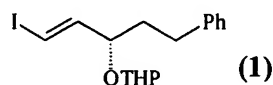
- 5 g) deprotecting the compound of formula (29) to provide Bimatoprost.

45. A process for synthesising Bimatoprost comprising the steps of:

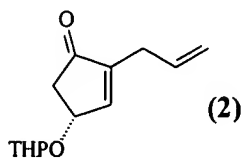
- a) preparing a compound of formula (3):



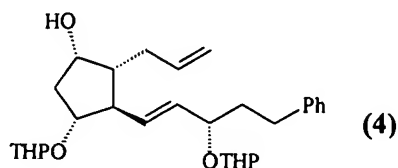
- 10 said preparing comprising converting a compound of formula (1):



to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):

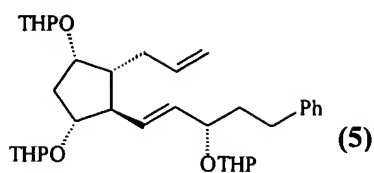


- 15 b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



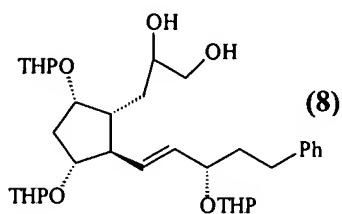
;

- c) protecting the compound of formula (4) to provide a compound of formula (5):



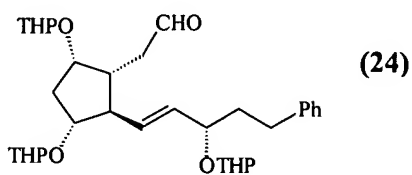
;

- d) dihydroxylating the compound of formula (5) to provide a compound of formula (8):



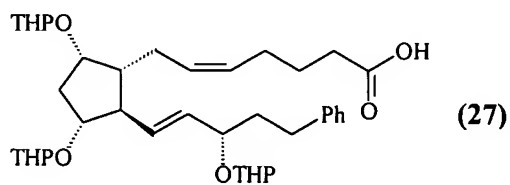
;

- 5 e) performing a diol cleavage reaction on the compound of formula (8) to provide a compound of formula (24):



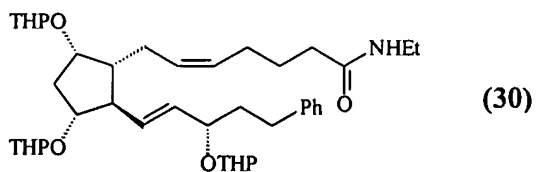
;

- f) performing a Wittig reaction on the compound of formula (24) to provide a
10 compound of formula (27):



;

- g) amidating the compound of formula (27) to provide a compound of formula (30):

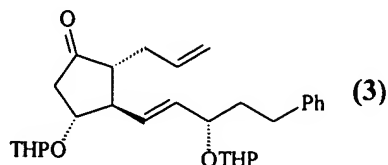


; and

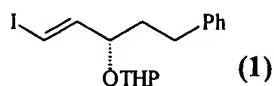
h) deprotecting the compound of formula (30) to provide Bimatoprost.

46. A process for synthesising Bimatoprost comprising the steps of:

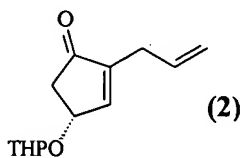
5 a) preparing a compound of formula (3):



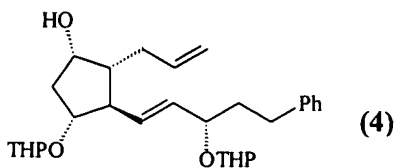
said preparing comprising converting a compound of formula (1):



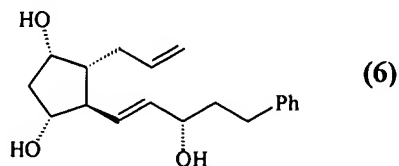
10 to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



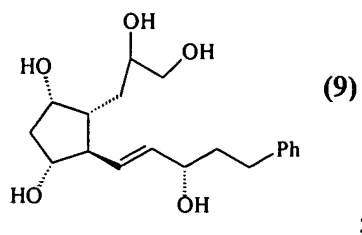
b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



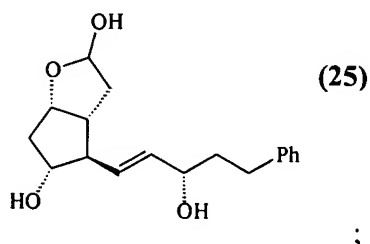
15 c) deprotecting the compound of formula (4) to provide a compound of formula (6):



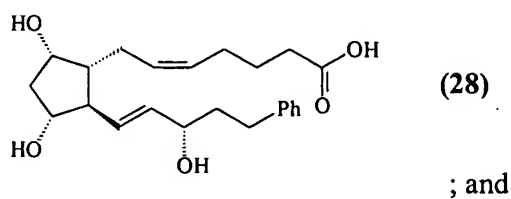
- d) dihydroxylating the compound of formula (6) to provide a compound of formula (9):



- 5 e) performing a diol cleavage on the compound of formula (9) to provide a compound of formula (25):



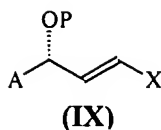
- f) performing a Wittig reaction on the compound of formula (25) to provide a compound of formula (28):
- 10



- g) amidating the compound of formula (28) to provide Bimatoprost.

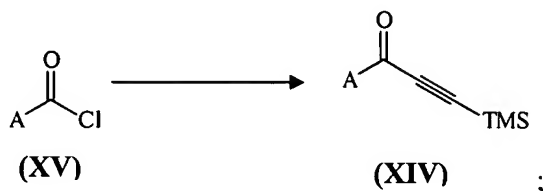
- 15 47. A process for synthesising Travoprost comprising a process according to any one of claims 1, 2, 7-8, 12-13, 17-18, 22-23, 29-30 and 34-35.

48. A process for synthesising a compound of formula (IX):

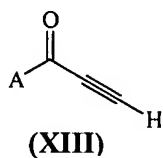


comprising the steps of:

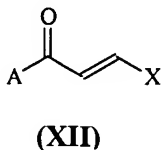
- a) reacting an acid chloride of formula (XV) with a bis(trialkylsilylacetylene) to form
5 an acetylene of formula (XIV):



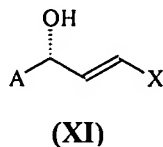
- b) reacting the acetylene of formula (XIV) with a reducing agent to form an
10 acetylene of formula (XIII):



- c) hydrohalogenating the acetylene of formula (XIII) to form a vinyl halide
15 comprising a prochiral ketone according to formula (XII);



- d) stereoselectively reducing the prochiral ketone in the vinyl halide of formula (XII)
to form a vinyl halide comprising a hydroxy group according to formula (XI); and



- e) protecting the hydroxy group in the vinyl halide of formula (XI) to provide the
20 compound of formula (IX);

wherein X is a halogen; P is a hydroxyl protecting group; and A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃.